

Comparison of dual chamber and ventricular rate responsive pacing in patients over 75 with complete heart block

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Abstract

Objective—To compare symptoms and exercise tolerance during dual chamber universal (DDD) and ventricular rate response (VVIR) pacing in elderly (≥ 75) patients.

Design—Randomised, double blind, crossover study.

Setting—Regional cardiac department.

Patients—Twenty elderly patients (mean age 80.5 (1) years) with high grade atrioventricular block and sinus rhythm. Patients with pre-existing risk factors for the pacemaker syndrome and chronotropic incompetence were excluded.

Intervention—After four weeks of VVI pacing following pacemaker implantation, patients underwent consecutive two week periods of VVIR and DDD pacing.

Main outcome measures—Patient preference, symptom scores, "daily activity exercises," and perceived level of exercise (Borg score).

Results—Eleven patients preferred DDD mode to either VVI or VVIR mode. Mean (SE) total symptom scores during VVI, VVIR, and DDD pacing were 5.9 (1.1), 6.1 (1.0), and 3.5 (0.9) respectively ($P < 0.01$). The corresponding mean (SE) pacemaker syndrome symptom scores were 4.8 (0.7), 5.2 (0.8), and 2.9 (0.8) ($P < 0.05$). Symptom scores during VVI and VVIR pacing were not significantly different. Exercise performance and Borg scores were significantly worse during VVI pacing compared with VVIR or DDD pacing but did not significantly differ between VVIR and DDD modes.

Conclusions—In active elderly patients with complete heart block both DDD and VVIR pacing are associated with improved exercise performance compared with fixed rate VVI pacing. The convenience and reduced cost of VVIR systems, however, may be offset by a higher incidence of the pacemaker syndrome. In elderly patients with complete heart block VVIR pacing results in suboptimal symptomatic benefit and should not be used instead of DDD pacing.

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pacemakers (DDD) should be considered for all patients with advanced atrioventricular block and sinus rhythm.¹ Compared with single chamber ventricular pacing (VVI), there are established benefits in haemodynamics,^{2,3} symptoms, and exercise performance.^{4,5} Single chamber rate responsive pacing (VVIR) has also been shown to improve haemodynamics⁶ and exercise performance^{7,8} compared with VVI pacing. It has therefore been suggested that in selected patients VVIR may be an acceptable alternative to DDD pacing.⁹ VVIR pacemakers are easier to insert than dual chamber systems and require less follow up: the rate response settings may need little attention after implantation.⁸ In addition, although atrial activity is not sensed, the rate response function ensures that exercise capacity is maintained at a level comparable with DDD pacemakers.⁹⁻¹¹ Finally, the average price of a VVIR system is considerably less than that of a DDD system. Potential disadvantages of VVIR pacing, however, include loss of atrial synchrony and development of the pacemaker syndrome.

One earlier study reported little subjective difference between DDD and VVIR pacing,⁹ but subsequent within patient comparisons have shown lower symptom scores and improved quality of life during DDD pacing compared with VVIR pacing.^{10,12,13} There is general agreement, however, that both DDD and VVIR modes lead to similar improvements in exercise tolerance.⁹⁻¹¹

In the United Kingdom the median age of patients referred for pacemaker implantation during 1993 was 76 years; 55% of all patients were aged over 75 years and 37% were aged over 80 years (British Pacing and Electrophysiology Group, personal communication). However, most patients enrolled in contemporary studies comparing VVIR and DDD pacing are under 75 years of age. Thus recommendations based on these studies may not necessarily be applicable to elderly patients with pacemakers. Age related changes in the cardiovascular system, for example, may render elderly people less tolerant of the loss of atrioventricular synchrony associated with VVIR pacing.¹⁴⁻¹⁶

The primary objective of the study was to compare symptoms and exercise tolerance during DDD and VVIR pacing in elderly patients with complete heart block. A secondary objective was to identify possible clinical or echocardiographic predictors of VVIR intolerance.

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Table 1 Characteristics of study patients

Case No	Sex	Age (years)	Other medical conditions	Drug treatment	Ejection fraction (%)
1	F	75	Claudication osteoarthritis	Aspirin	40
2*†	M	75	None	None	72
3	M	83	Osteoarthritis	None	50
4	M	83	Asthma, hypertension, previous mild stroke	Bronchodilators, aspirin	53
5	M	80	Hypertension, acromegaly	Co-amilofruse	77
6†‡	M	84	None	None	65
7	M	75	Emphysema	Bronchodilators, steroids	59
8†‡	M	83	Gout, hypertension	Nifedipine	65
9†	F	75	Angina	None	78
10	M	81	None	None	62
11	F	86	Hypertension	Nifedipine, bendrofluazide	n/a
12	M	80	Rheumatoid arthritis, diabetes	None	65
13	F	81	Hypertension	Enalapril	60
14‡	M	77	Diabetes	None	n/a
15	M	89	Osteoarthritis, hypertension	Enalapril, bendrofluazide	63
16	F	75	None	None	75
17‡	M	85	Mild asthma	Bronchodilators	n/a
18	M	84	Gout	None	53
19	M	83	Osteoarthritis	None	55
20	F	76	None	None	58

*Developed retrograde conduction. †Requested early crossover for VVIR.

‡Developed 1:1 anterograde atrioventricular conduction before first visit.

Patients and methods

We studied 20 consecutive patients aged 75–89 (mean 80.5 (1.0) years; 14 men) who had been referred for permanent pacemaker implantation. Patients were eligible if (a) they were aged over 75, (b) an electrocardiogram before implantation showed sinus rhythm and complete heart block of at least 7 days' duration, and (c) they had previously been able to carry out independently the daily activity tests described below. Exclusion criteria included pre-existing indications for the maintenance of atrial synchrony—for example, left ventricular dysfunction—evidence of retrograde atrioventricular conduction at implantation, and chronotropic incompetence. Informed consent was obtained from each patient, and the study was approved by the local research ethics committee. Basic demographic data are presented in table 1.

STUDY DESIGN

The study was a double blind, two period, crossover comparison of DDD and VVIR pacing modes. Eligible patients received a Biotronic Ergos 03 dual chamber pacemaker (DDDR) and were discharged from hospital with it in VVI pacing mode. After a month each patient returned to be assessed by questionnaire and to undertake exercise testing in VVI mode in order to familiarise themselves with the study protocol and provide baseline data. Patients also underwent a symptom limited treadmill test (modified Bruce protocol) in DDD pacing mode to assess the chronotropic response to exercise.¹⁷ Patients with chronotropic incompetence were withdrawn. Patients were then randomly allocated either VVIR or DDD pacing (mode 1). After two weeks their response to mode 1 was assessed by questionnaire and exercise testing before their pacemakers were reprogrammed to the alternative mode (mode 2). At the final visit exercise testing and questionnaires were repeated and the patients were asked which study period, if any, they had preferred. Finally, patients were returned to DDD mode and echocardiography was performed. The ejection fraction was calculated by the area-length method.¹⁸

PACEMAKER PROGRAMMING

In all three modes the lower and upper rates were set, when applicable, at 72 and 125 beats/minute respectively.¹⁹ The a-v delay was set at 175 ms. In VVIR mode the rate response threshold was set at medium and the curve between 6 and 8. The final setting was determined by the sinus response during treadmill exercise (visit 1).

SYMPTOM QUESTIONNAIRES

At each visit patients were asked by questionnaire whether they had experienced symptoms during the preceding two weeks and, if so, to what extent.²⁰ Symptoms suggestive of the pacemaker syndrome (breathlessness, pulsation, dizziness, blackout, wheeze, fatigue, palpitation, and cough) were included in a list with control symptoms (headache, chest pain, diarrhoea, vomiting, apprehension, leg cramps, cough, dysuria). Patients were asked to indicate the severity of each symptom on an analogue scale marked from 0 to 5 (0, none; 1, very mild; 2, mild; 3, moderate; 4, quite severe; 5, very severe).

EXERCISE TESTING

At each visit patients underwent three simple exercise tests corresponding to the daily activities of elderly patients. The exercises were supervised by the same investigator for each patient and followed the same order.

(1) Stand ups from a chair. Patients were asked to stand up and sit down from a standard chair as many times as possible for two minutes.

(2) Walking. Patients walked as briskly as possible back and forth along a measured length (approximately 25 m) of corridor, turning around at the end of each length. The total number of lengths walked in six minutes, or the maximum number attained by the patient before asking to stop, was recorded.

(3) Stair climbing. Patients were timed how quickly they could ascend two flights of stairs (26 steps), using a stair rail if necessary.

The heart rate at peak exercise was determined immediately after exercise by an automated heart rate monitor. Patients were asked to grade how difficult they had perceived each

Table 2 Effect of pacing order on symptom scores, exercise performance, and total Borg scores. Values are means (SE)

	Pacing order (11 patients):			Pacing order (9 patients):		
	VVI	DDD	VVIR	VVI	VVIR	DDD
Symptom score:						
Total	6.5 (2)	3.6 (1)*	7.6 (1)	5.0 (1)	4.6 (1)	3.4 (1)
Pacemaker syndrome	4.7 (1)	2.9 (1)*	6.3 (1)	4.7 (1)	3.9 (1)	2.7 (2)
Exercise performance:						
No of stand ups in 2 minutes	36 (4)**	44 (5)	43 (6)	35 (5)†	40 (5)	42 (5)
No of lengths walked in 6 minutes	18 (2)	20 (1)	20 (1)	18 (2)	18 (2)	20 (2)
Time to climb 26 steps(s)	15 (1)	14 (1)*	15 (1)	19 (3)	17 (2)	16 (3)
Total Borg score	37 (1)	34 (2)	37 (1)	35 (2)	35 (2)	33 (2)

*Significantly different from VVI and VVIR; **significantly different from VVIR and DDD; †significantly different from DDD ($P < 0.05$).

exercise according to the Borg symptom score, scores being from 6 (very, very light) to 20 (very, very hard) with corresponding word prompts for the numbers in between.

STATISTICAL ANALYSIS

All results are expressed as means (SE). Means were compared by an analysis of variance. The differences between means were detected by Fisher's least significant difference test. A P value less than 0.05 was regarded as significant. The study size was calculated from data derived from a previous investigation.²⁰ With type I and II errors set at 0.1 and 0.05 respectively there was sufficient power to detect a four point change in pacemaker symptom score, a 20% change in total Borg score, and a 25% change in exercise capacity. The study was analysed on an intention to pace basis; we included patients who developed spontaneous return of anterograde conduction, but we also performed an analysis excluding them.

Results

Four patients spontaneously regained anterograde atrioventricular conduction between pacemaker implantation and the initial study visit. In these patients the pacemaker was inhibited by the resting sinus rate during VVI

mode. In two of these patients the ventricles were paced during exercise in VVIR mode, resulting in the development of the pacemaker syndrome.

One patient developed retrograde conduction during the VVIR study that was associated with significant symptomatic deterioration. Three patients requested early crossover from VVIR pacing owing to intolerable symptoms. Overall, 11 patients preferred DDD mode to the other two modes. One patient each preferred VVI and VVIR mode and seven did not express a preference.

The mean period effect on total symptom and pacemaker syndrome symptom were 1.4 and 1.1 respectively ($P > 0.05$). There was no significant treatment and period interaction. The effects of pacing order—that is, DDD followed by VVIR or vice versa—on symptom scores, exercise performance, and Borg scores are shown in table 2. Symptomatically, patients tolerated VVIR pacing better if they had not been previously exposed to DDD pacing. Exercise tolerance and Borg scores, however, were not influenced by the order of pacing.

SYMPTOMS

Mean total symptom scores during VVI, VVIR, and DDD pacing were 5.9 (1.1), 6.1 (1.0), and 3.5 (0.9) respectively ($P < 0.01$). The corresponding pacemaker syndrome symptom scores were 4.8 (0.7), 5.2 (0.8), and 2.9 (0.8) ($P < 0.05$). The scores for individual patients are shown in figure 1. Both scores were significantly reduced during DDD mode compared with VVI and VVIR modes ($P < 0.05$). Symptom scores during VVI and VVIR modes were not significantly different. When the four patients with anterograde atrioventricular conduction were excluded the total symptom scores were 6.8 (1.3), 6.3 (1.1) and 3.9 (1.0) for VVI, VVIR, and DDD modes respectively ($P < 0.01$). The corresponding pacemaker syndrome symptom scores were 5.4 (0.8), 5.4 (0.9), and 3.3 (0.9) ($P < 0.05$).

EXERCISE PERFORMANCE AND PERCEIVED EXERCISE DIFFICULTY

For each test, exercise performance was better in the rate-response modes (DDD and VVIR) than with VVI pacing. In contrast to symptom scores, exercise performance during DDD and VVIR modes was similar. Maximum heart rates after each exercise were similar in the two rate-response modes. These results are detailed in tables 3 and 4.

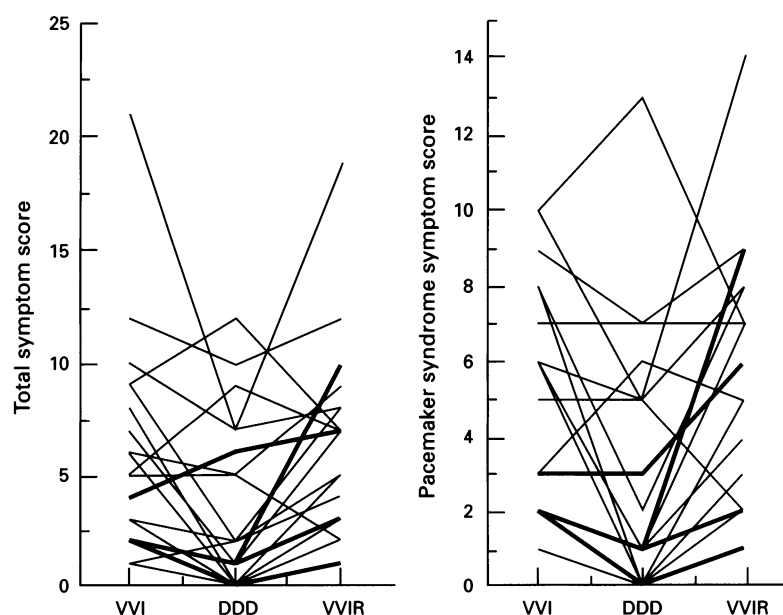


Figure 1 Individual total symptom and pacemaker syndrome symptom scores during VVI, DDD, and VVIR pacing. Thickened lines represent patients with intact anterograde atrioventricular conduction.

Table 3 Exercise test performances and respective Borg scores during VVI, VVIR, and DDD pacing modes. Values are means (SE)

Mode	Stand ups		Walking		Climbing 26 steps	
	No	Borg score	No of lengths	Borg score	Time(s)	Borg score
VVI	35 (3)*	13 (1)	18 (1)*	12 (1)	17 (1)	11 (1)
VVIR	41 (4)	13 (1)	19 (1)	11 (1)	16 (1)	12 (1)
DDD	42 (3)	12 (1)	20 (1)	11 (1)	15 (1)**	11 (1)

*Significantly different from VVIR and DDD mode ($P < 0.05$).

**Significantly different from VVI ($P < 0.01$).

Total Borg scores (SE) during VVI, VVIR, and DDD modes were 35.7 (1.3), 33.5 (1.4), and 35.8 (1.1) respectively ($P = 0.06$). The Borg values for each exercise test are shown in table 3.

ECHOCARDIOGRAPHIC DATA

Echocardiographic data were available in 17 patients. Mean (SE) left ventricular systolic and diastolic dimensions were 34.9 (1.5) mm and 54.2 (1.2) mm respectively. The mean ejection fraction was 61.8% (2.5%). There was a significant correlation between resting ejection fraction (DDD mode) and total ($r^2 = 0.38$, $P < 0.01$) and pacemaker symptom ($r^2 = 0.29$, $P < 0.05$) scores during baseline VVI pacing (fig 2). However, the association was not strong enough to allow accurate prediction of VVI intolerance or preference. Mean left atrial size was 38 (1.1) mm (range 32–49 mm). There was no correlation between left atrial size and any symptom score or derivative.

Discussion

In our elderly population both total and pacemaker syndrome symptom scores were significantly lower during DDD mode compared with VVI and VVIR modes. There was no difference in symptom scores between VVI and VVIR pacing modes. In terms of exercise performance and the perceived level of exercise (Borg score), however, we observed no overall difference between the two rate-response modes. Both rate-response modes (DDD and VVIR) were significantly better than baseline VVI pacing.

Figure 2 Relation between resting ejection fraction (DDD mode) and total symptom score during VVI mode

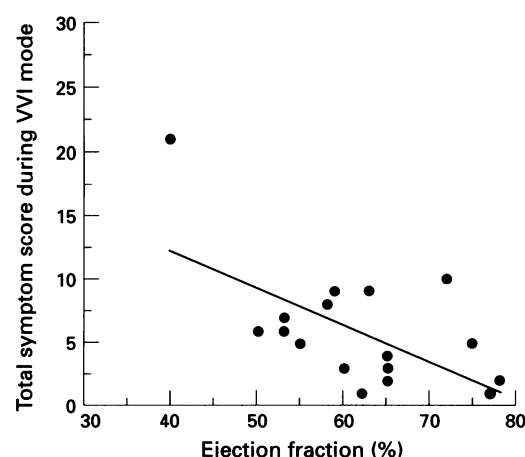


Table 4 Mean (SE) heart rates (beats/minute) during VVI, VVIR, and DDD pacing modes for each exercise

Exercise	VVI	VVIR	DDD
Stand ups	82 (5)*	106 (4)	107 (4)
Walking	80 (3)*	113 (3)	109 (4)
Climbing stairs	81 (4)*	112 (3)	111 (4)

*Significantly different from VVIR and DDD, ($P < 0.001$).

SYMPTOM SCORES

Previous crossover studies within patients have compared symptoms and exercise performance during DDD and VVIR pacing modes. Sulke *et al* reported symptomatic deterioration during VVIR compared with DDD pacing within a fairly young population (mean age 52 (4)).¹¹ Menozzi *et al* likewise reported significant symptomatic deterioration during VVIR pacing in a group of older patients (mean age 72 (6)).¹⁰ In this study there was substantial variation in the individual responses to VVIR pacing; five (36%) patients reported severe symptoms and requested early crossover while a further six (43%) reported no difference between the two pacing modes.¹⁰ In contrast, we found that most of our patients (80%) reported deterioration in symptoms during VVIR compared with DDD pacing. One of the patients who reported improved symptoms during VVIR pacing had significant obstructive airways disease and was aware of an uncomfortable resting tachycardia (sinus rate 100 beats/minute) when atrial tracking (DDD mode). His symptomatic tachycardia, presumably related to his regular bronchodilator treatment, was abolished during VVIR pacing.

The subjective response to VVIR pacing was highly dependent on whether there had been previous exposure to dual chamber pacing. For example, in the 11 patients who had been randomly allocated DDD mode then VVIR mode we observed substantial symptomatic deterioration when these patients were re-exposed to single chamber pacing (VVIR). Seven of the 11 patients who preferred DDD mode came from this group, along with two of the three patients who requested early crossover from VVIR mode. In contrast, nine patients initially exposed to VVIR pacing reported symptomatic improvement compared with baseline VVI. These observations are similar to those of Sulke *et al*, who compared VVI, DDI, and DDD pacing modes in a group of apparently symptom free patients with long term VVI pacemakers.²¹ We also observed that exercise tolerance was not significantly influenced by the pacing order. Freed from the worry of syncope after having had a pacemaker implanted, most patients are much improved with simple VVI pacing. Although some patients will develop overt pacemaker syndrome, most will remain without complaint, unaware of the symptomatic benefits associated with physiological (dual chamber) pacing. It is only after exposure to dual chamber pacing that the high incidence of subclinical pacemaker syndrome in these patients becomes apparent.²¹

Oldroyd *et al* observed no difference in overall symptoms between DDD and VVIR pacing modes in 10 patients (mean age 56; range 23–74).⁹ Important age related cardiovascular changes may render elderly people less tolerant of non-physiological—that is, VVIR pacing. Left ventricular compliance decreases with advancing age,¹⁴ increasing the dependence of cardiac output on atrial filling during late diastole.¹⁵ Corrective cardiovascular reflexes, such as the baroreflexes, may be attenuated with advancing age, thereby increasing the risks of hypotension and of the pacemaker syndrome.¹⁶ In the studies by Sulke *et al*¹⁰ and Menozzi *et al*¹¹ and in our study, the symptom questionnaire was specifically designed to detect symptoms suggestive of the pacemaker syndrome—for example, palpitations, pulsation, and dizziness—whereas the questionnaire (McMaster) used in Oldroyd's study does not specifically ask about the pacemaker syndrome and may have underestimated these symptoms.

Anterograde atrioventricular conduction returned in four (20%) patients after implantation. Although comfortable at rest, two of these patients experienced palpitations and dyspnoea (the pacemaker syndrome) during exercise in VVIR mode but not in DDD mode. In these circumstances the pacemaker syndrome arises when the rate-response function drives the ventricular rate higher than the natural sinus rate.^{22–23} Despite symptoms of exercise induced pacemaker syndrome, the overall exercise tolerance of these patients was similar to that during DDD mode. Exclusion of these patients from the analysis did not significantly change the overall findings of the study.

EXERCISE PERFORMANCE

Our observations confirm previous reports of improved exercise capacity in the elderly during either DDD^{20–24} or VVIR pacing modes⁸ compared with fixed rate VVI pacing. However, most studies that have directly compared DDD and VVIR modes have reported no significant difference in exercise performance.^{9–10} The contribution of atrial filling to stroke volume increases with advancing age, particularly so during submaximal exercise,²⁵ and we had hypothesised that both exercise performance and the perceived level of exercise (Borg scores) in our group of elderly patients would be improved during DDD pacing compared with VVIR pacing. Although we found a trend towards a benefit from DDD pacing, the difference was not significant.

Failure to detect an important difference is unlikely to be a type II error since the power of the sample size was sufficient to detect at least a 25% change in the performance of each test. Neither can these observations be explained by the exercise heart rates as these were well matched for each test. Alternatively, the findings may be partly explained by a selection bias which favoured enrolment of comparatively fit elderly subjects with more cardiovascular reserve who were able to com-

pensate for the loss of atrial contraction during VVIR pacing. Patients in whom there was considered to be a relatively strong indication for dual chamber pacing—for example, a history of heart failure—were not recruited, as borne out by the normal echocardiographic left ventricular dimensions. Selection bias towards fitter elderly patients may also have resulted from the study design, which required three separate visits to the department and extended travelling distances.

RETROGRADE ATRIOVENTRICULAR CONDUCTION

The development of retrograde atrioventricular conduction in one of our patients (during VVIR mode pacing) was heralded by significant deterioration in symptoms. Similarly, in the study of Oldroyd *et al* the only patient to request early crossover from VVIR to DDD mode was the only patient with intact retrograde conduction.⁹ The nine other patients without retrograde conduction reported no deterioration in symptoms during VVIR pacing. The authors concluded “that it would be appropriate to consider VVIR activity sensing pacemakers . . . in patients with complete anterograde and retrograde heart block and preserved ventricular function.”⁹ Although retrograde conduction may be a risk factor for the development of the pacemaker syndrome,²⁶ the absence of retrograde conduction at pacemaker implantation does not preclude its subsequent development.^{27–28} Furthermore, the presence of ventriculoatrial conduction has limited utility as a predictor of the pacemaker syndrome in individual patients.^{11–20}

CLINICAL IMPLICATIONS

In active elderly patients with complete heart block both DDD and VVIR pacing are associated with improved exercise performance compared with fixed rate VVI pacing. Although VVIR pacing may be adequate in some patients, the convenience and reduced cost of these systems may be offset by the high incidence of the pacemaker syndrome. On the basis of these observations we conclude that VVIR pacing in elderly subjects with complete heart block results in suboptimal symptomatic benefit and should not be used instead of DDD pacing.

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